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(19) **United States**(12) **Patent Application Publication** (10) **Pub. No.: US 2006/0223120 A1****Kim et al.**(43) **Pub. Date: Oct. 5, 2006**(54) **HIGH-THROUGHPUT METHOD FOR  
OPTIMUM SOLUBILITY SCREENING FOR  
HOMOGENEITY AND CRYSTALLIZATION  
OF PROTEINS****Publication Classification**(51) **Int. Cl.**  
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(52) **U.S. Cl.** ..... **435/7.1; 702/19**(76) Inventors: **Sung-Hou Kim**, Moraga, CA (US);  
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(US)(57) **ABSTRACT**

Herein is described and optimum solubility screen in which a panel of buffers and many additives are provided in order to obtain the most homogeneous and monodisperse protein condition for protein crystallization. The present methods are useful for proteins that aggregate and cannot be concentrated prior to setting up crystallization screens. A broad range of buffers is intended for use in this screen. A high-throughput method using the hanging-drop method and vapor diffusion equilibrium and a panel of twenty-four buffers is further provided. After monitoring precipitation, the conditions leading to clear drops are selected for evaluation, preferably dynamic light scattering (DLS) characterization. If the DLS results are not optimal, a series of additives are tested in the presence of the best buffer selected from the initial screen and again DLS is used to determine the best condition. Using the present methods, 14 poorly behaving proteins have been screened, resulting in 11 of the proteins having highly improved DLS results allowing concentration of the proteins, and 9 were crystallized.

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